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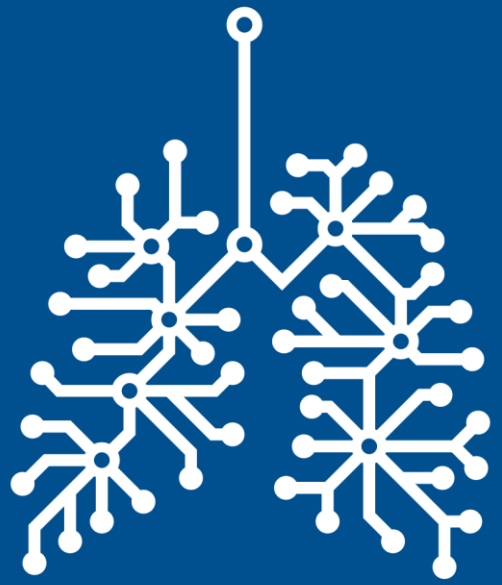

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Dupilumab Long-Term Safety and Efficacy in Patients With Asthma: LIBERTY ASTHMA TRAVERSE

Michael E. Wechsler[1], Linda B. Ford[2], Jorge F. Maspero[3], Ian D. Pavord[4], Yuji Tohda[5], David Langton[6], Christian Domingo[7], Alberto Papi[8], Arnaud Bourdin[9], Henrik Watz[10], Hae Sim Park[11], Kenneth R. Chapman[12], Xuezhou Mao[13], Benjamin Ortiz[14], Michel Djandji[15], Upender Kapoor[13], Faisal A. Khokhar[14], Leda P. Mannent[16], Marcella Ruddy[14], Elizabeth Laws[13], Nikhil Amin[14], Megan Hardin[15]

[1]National Jewish Health, Denver, CO, USA; [2]Asthma & Allergy Center, Bellevue, NE, USA; [3]Fundación CIDEA, Buenos Aires, Argentina; [4]University of Oxford, Oxford, UK; [5]Kindai University, Osakasayama, Osaka, Japan; [6]Frankston Hospital, Frankston, VIC, Australia; [7]Corporació Sanitària Parc Taulí, Sabadell, Barcelona, Spain; [8]Respiratory Medicine Unit, University of Ferrara, S. Anna University Hospital, Ferrara, Italy; [9]Université de Montpellier, CHU Montpellier, PhyMedExp, INSERM, CNRS, Montpellier, France; [10]Pulmonary Research Institute, LungenClinic Grosshansdorf, Airway Research Center North (ARCN), German Center for Lung Research (DZL), Grosshansdorf, Germany; [11]Ajou University, Suwon, South Korea; [12]University of Toronto, Toronto, ON, Canada; [13]Sanofi, Bridgewater, NJ, USA; [14]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [15]Sanofi, Cambridge, MA, USA; [16]Sanofi, Chilly-Mazarin, France

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Background and aim

- Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for IL-4 and IL-13, key and central drivers of type 2 inflammation in multiple diseases[1–4]

- The efficacy and safety of dupilumab up to 1 year have been demonstrated
  - In the phase 2b DRI (P2b; NCT01854047)[5] and phase 3 QUEST (NCT02414854)[6] studies, add-on dupilumab 200 mg and 300 mg q2w, vs placebo, significantly reduced severe asthma exacerbations and improved pre-BD FEV_1 in patients with uncontrolled, moderate-to-severe asthma with greater treatment effects in patients with elevated type 2 biomarkers at baseline

Aim

- **To evaluate the long-term safety, tolerability, and efficacy of dupilumab in an open-label extension study (NCT02134028) of patients with asthma who completed a previous dupilumab asthma clinical study (P2b, phase 3 QUEST, phase 2a EXPEDITION [NCT02573233], or phase 3 VENTURE [NCT02528214])**

BD, bronchodilator; FEV_1, forced expiratory volume in 1 second;
IL, interleukin; q2w, every 2 weeks.

LIBERTY ASTHMA TRAVERSE open-label extension study (NCT02134028) study design

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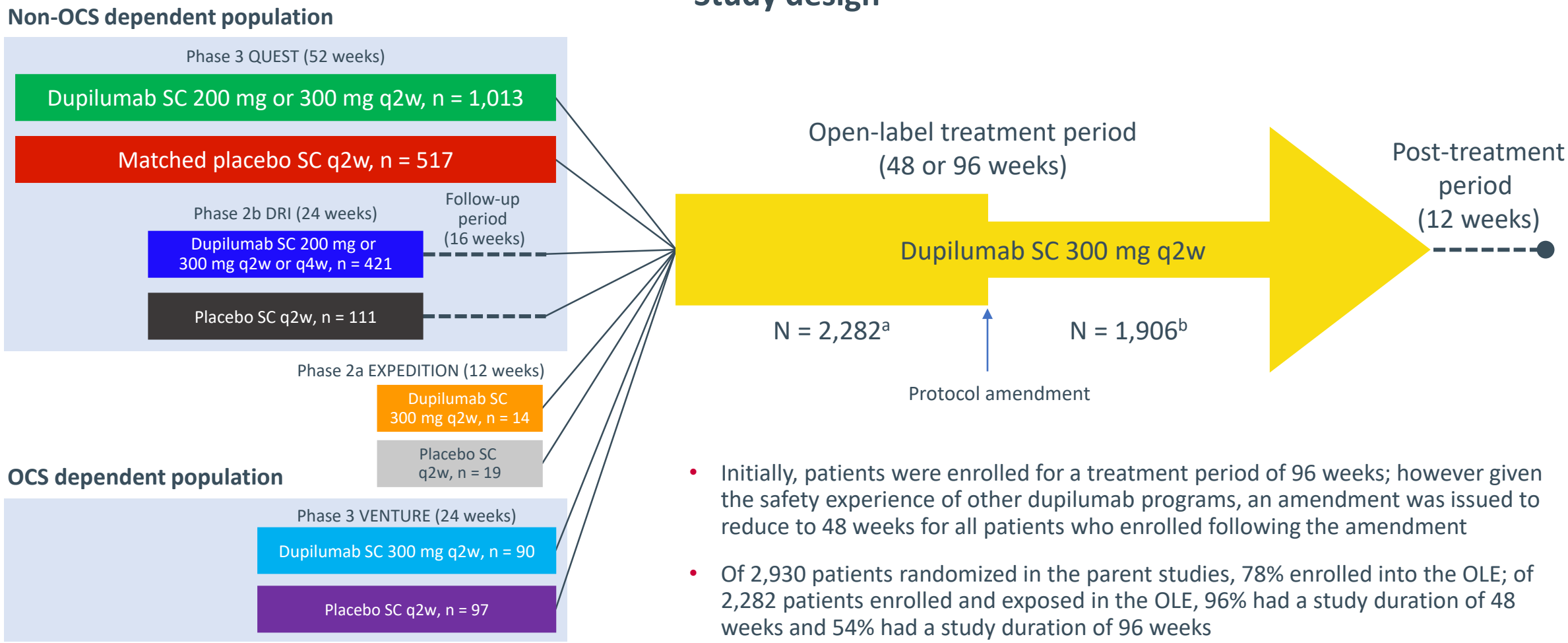
Study design



- Initially, patients were enrolled for a treatment period of 96 weeks; however given the safety experience of other dupilumab programs, an amendment was issued to reduce to 48 weeks for all patients who enrolled following the amendment
- Of 2,930 patients randomized in the parent studies, 78% enrolled into the OLE; of 2,282 patients enrolled and exposed in the OLE, 96% had a study duration of 48 weeks and 54% had a study duration of 96 weeks

Patient numbers presented for parent studies represent the number of patients who enrolled into and were exposed to treatment in the OLE. [a]Total number of patients enrolled and exposed to treatment in the OLE. [b]Total number of patients who continued to be exposed to treatment beyond 48 weeks. OCS, oral corticosteroid; OLE, open-label extension; q4w, every 4 weeks; SC, subcutaneous.

Rates of TEAEs in the OLE were similar to those observed in the parent studies[5–7] with no new safety signals identified

- Rates of TEAEs in the overall ITT populations of the parent studies, P2b, QUEST, and VENTURE, were 75–83%, 81–83%, and 62–64%, respectively[5–7]

OLE outcomes	Patients from P2b		Patients from QUEST		Patients from VENTURE	
	Placebo/dupilumab[a] (n = 111)	Dupilumab/dupilumab[b] (n = 421)	Placebo/dupilumab[a] (n = 517)	Dupilumab/dupilumab[b] (n = 1,013)	Placebo/dupilumab[a] (n = 97)	Dupilumab/dupilumab[b] (n = 90)
Patients with any TEAE						
n (%)	88 (79.3)	369 (87.6)	414 (80.1)	789 (77.9)	74 (76.3)	70 (77.8)
nP/PY (nP/100 PY)[c]	88/72.5 (121.4)	369/228.7 (161.4)	414/293.6 (141.0)	789/613.6 (128.6)	74/57.0 (129.8)	70/53.8 (130.0)
Patients with any treatment-emergent SAE						
n (%)	14 (12.6)	42 (10.0)	48 (9.3)	106 (10.5)	12 (12.4)	10 (11.1)
nP/PY (nP/100 PY)[c]	14/207.0 (6.8)	42/794.2 (5.3)	48/747.9 (6.4)	106/1457.6 (7.3)	12/125.3 (9.6)	10/119.4 (8.4)
Patients with any TEAE leading to death						
n (%)	0	3 (0.7)	0	1 (< 0.1)	0	0
nP/PY (nP/100 PY)[c]	0/222.3	3/827.6 (0.4)	0/780.5	1/1543.4 (< 0.1)	0/137.6	0/124.8
Patients with any TEAE leading to permanent treatment discontinuation						
n (%)	3 (2.7)	19 (4.5)	12 (2.3)	31 (3.1)	4 (4.1)	5 (5.6)
nP/PY (nP/100 PY)[c]	3/221.5 (1.4)	19/822.4 (2.3)	12/777.1 (1.5)	31/1534.4 (2.0)	4/136.4 (2.9)	5/123.5 (4.0)

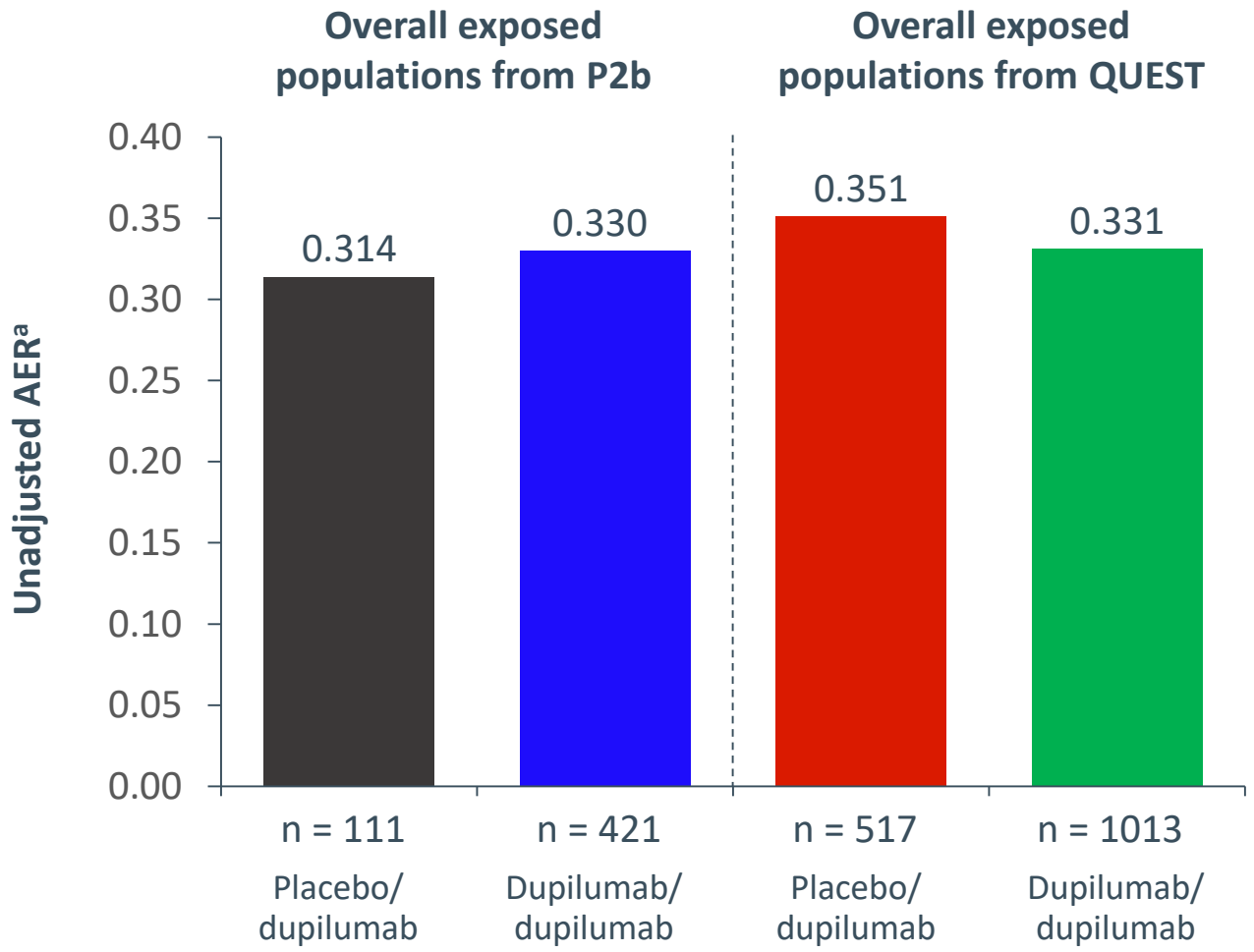
- The most common TEAEs occurring in any treatment group during OLE were nasopharyngitis and injection-site erythema, 9–13% of patients experienced SAEs, the number of patients with TEAE leading to permanent discontinuation was low and 4 deaths occurred (metastatic lung cancer, adenocarcinoma gastric, craniocerebral injury, and respiratory failure)

[a]Patients who had been in the placebo arms of the parent studies and then exposed to dupilumab 300 mg q2w in the OLE. [b]Patients who had been in the dupilumab arms of the parent studies and exposed to dupilumab 300 mg q2w in the OLE.
[c]For patients with event, PY are calculated up to the date of the first incidence; for patients without event, PY correspond to the length of study observation period.

ITT, intent-to-treat; MedDRA, Medical Dictionary for Regulatory Activities; n (%), number and percentage of patients with ≥ 1 TEAE; nP, number of patients with any event; nP/100 PY, number of patients with ≥ 1 event per 100 patient-years; PY, patient-years; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

In non-OCS dependent patients, the low unadjusted annualized exacerbation rate observed in the parent studies[5–7] were sustained during the OLE

- At parent study baseline for P2b and QUEST, mean number of exacerbations in the past year across treatment groups in the overall ITT populations were 1.85–2.37 and 2.02–2.31, respectively[5,6]
- At end of parent study treatment, unadjusted AER for placebo- and dupilumab-treated patients were 1.07 and 0.31–0.69 for P2b and 0.98–1.09 and 0.48–0.56 for QUEST, respectively
- During the OLE, unadjusted AER ranged from 0.31–0.35 in the non-OCS dependent population



[a]The total number of events that occurred during the treatment period divided by the total number of patient-years followed in the treatment period. AER, Annualized severe exacerbation rate.

In non-OCS dependent patients, improvements in FEV_1 observed in the parent studies[5–7] were sustained during the OLE

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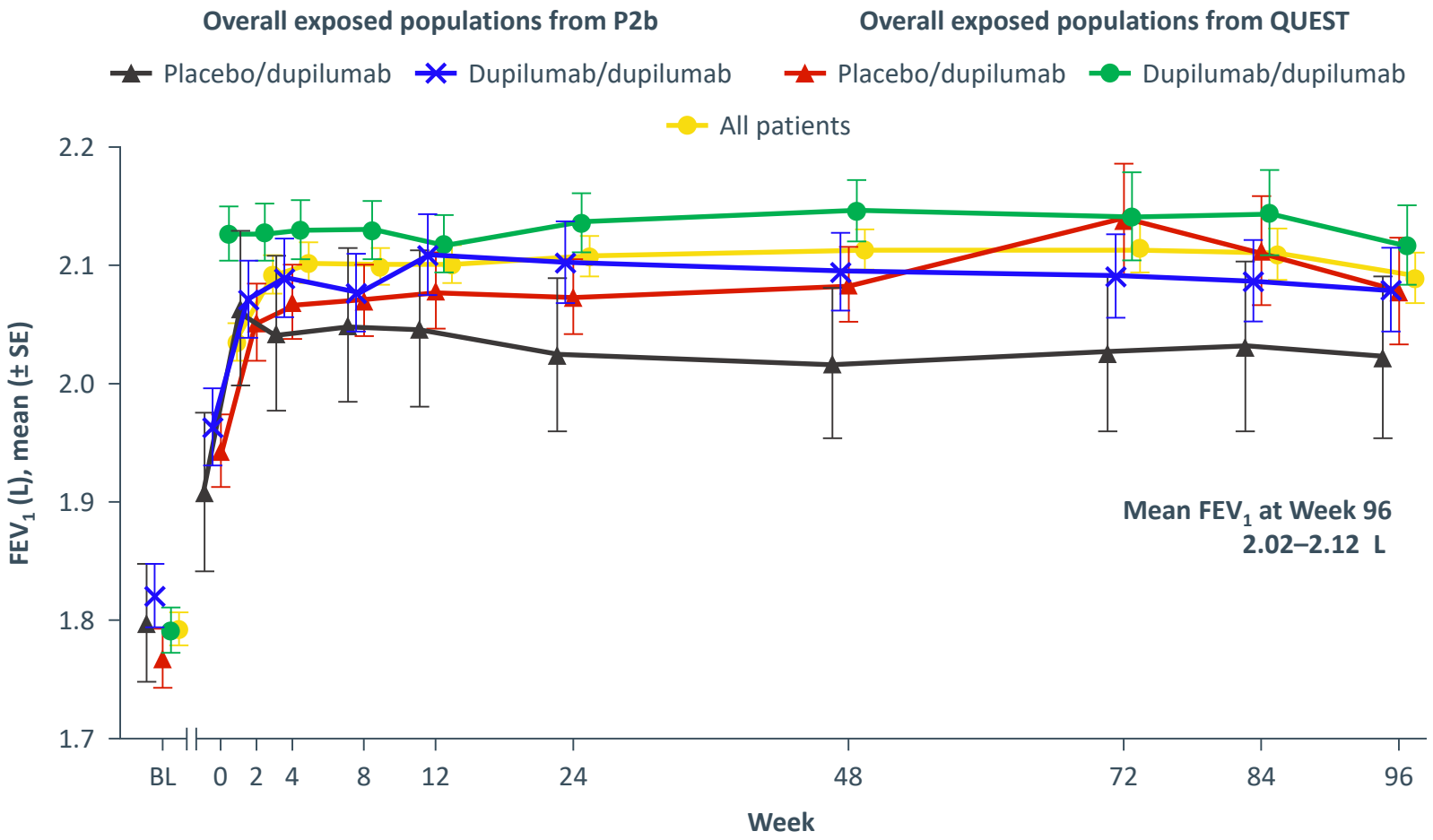
- At parent study baseline for P2b and QUEST, mean FEV_1 across treatment groups in the overall ITT populations was 1.79–1.86 and 1.75–1.78 L, respectively[5,6]
- At end of parent study treatment, mean FEV_1 for placebo- and dupilumab-treated patients was 1.99 and 2.11–2.15 L for P2b and 1.89–1.94 and 2.13 L for QUEST, respectively[5,6]
- At Week 96 of the OLE, mean FEV_1 was 2.02–2.12 L (13%–22% mean percent change from parent study baseline) in the non-OCS dependent population



No. of patients											
Patients from P2b, placebo/dupilumab	111	111	108	111	110	110	109	105	104	102	102
Patients from P2b, dupilumab/dupilumab	421	421	412	415	410	415	409	396	383	379	380
Patients from QUEST, placebo/dupilumab	517	516	498	503	483	497	497	486	221	218	219
Patients from QUEST, dupilumab/dupilumab	1013	1010	978	980	962	977	972	951	447	444	447
All patients	2062	2058	1996	2009	1965	1999	1987	1938	1155	1143	1148

BL represents the baseline of the parent study, Week 0 represents the start of the OLE, and Weeks refer to the time in OLE without regard to any time in any parent study. BL, baseline; SE, standard error.

Conclusions

- Long-term treatment of adult and adolescent moderate-to-severe asthma patients with dupilumab 300 mg q2w was generally well tolerated, with a long-term safety profile that was consistent with that seen in the shorter duration parent studies, P2b, QUEST and VENTURE[5–7]

- Long-term treatment of adult and adolescent, non-OCS dependent, moderate-to-severe asthma patients with dupilumab demonstrated maintenance of the clinical efficacy that was observed in the parent studies, P2b and QUEST,[5,6] including a persistently low exacerbation rate and sustained improvements in lung function up to 96 weeks

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